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[Reports to the Supervising Surgeon-General United States Marine-Hospital Service.]

The bubonic plague bacillus as studied at the Pasteur Institute.

[Continued.]

77-79 RUE NOTRE DAME DES CHAMPS,
Paris, France, June 14, 1897.

SIR: I have the honor to submit the following for your consideration, concerning the epidemic of plague in Bombay and Kerachi, most of the information being derived from the reports of Dr. Yersin to the Institute Pasteur, and imparted by Professor Roux in an address delivered at the weekly reunion of the workers at the institute:

Mortality.—From the most reliable information collected from all sources, it would seem that the average mortality in this epidemic in India has reached the appalling figure of 90 to 95 per cent of those attacked. This is open to some doubt, as the Hindoos have displayed an aversion to treatment in hospitals, and compulsory removal to these institutions having been adopted as a rule, many cases occurring among the native population have been concealed, and do not appear in the total of cases or deaths. The mortality as reported is, therefore, probably rather below than above the truth. It will also be understood that these figures do not include those subjected to serum therapy, of which special mention will be made in another portion of this summary.

Types of the disease.—For convenience of classification, and in accordance with the clinical symptoms presented, the disease in this epidemic has been classified as (a) bubonic, or ganglionic; (b) septicæmic; (c) pneumonic. Of these forms the bubonic has been the most common; the pneumonic the most fatal. The method of infection, that is to say the point of entrance of the specific microbe, is a point still under active discussion, and is different not only for the various types and forms

given, but also varies in different countries and in different sections of the same country. For example, in Hongkong, where the natives as a rule go barefooted, infection in a large number of cases has been traced to abrasions and wounds of the lower extremities; in India, some covering or protection for the foot is usually worn, but the natives suffer from the bites of insects and vermin, consequently the point of entrance of the infection has been largely upon the hands and arms. Infection through the intestinal or respiratory tract, while admitted, is as yet largely unexplained, for, in spite of the assertions of Wilm, some breach of continuity would seem to be necessary for the entrance of the micro-organism. As a rule, a small red spot marks the point of infection; this becomes successively a vesicle and a pustule, and in the ganglionic form, and in a large proportion of cases a general redness or a series of vesicles marks the passage of the infection along a lymphatic tract or channel. These vesicles have been of very frequent occurrence in the Bombay epidemic.

Symptoms and course.—In the bubonic form the victim is seized with a chill, followed by a fever of greater or less intensity, sometimes reaching 41° to 42° C.; there is an overwhelming prostration; nausea and vomiting and the rapid formation of a glandular enlargement, surrounded by an extensive oedema, forming the bubo which has given the most common name to the disease. The bubo may or may not break down and go on to suppuration. If it does the ganglionic form merges into the septicæmic, without any distinct line of demarkation between the two types. Early in the disease stupor, delirium, and a more or less profound unconsciousness mark the existence of an intoxication or general systemic infection.

In the septicæmic form it would seem that the infection has taken place through the intestinal, digestive, or respiratory passages, or has been secondary to the suppuration of a bubo. These cases are as a rule not as violent in their course as the other types, and furnish the larger portion of the small number of recoveries. The pneumonic form is at once the most insidious in its onset, the most difficult of diagnosis, and the most fatal in its results. It is usually ushered in by a pain in the side, which becomes more pronounced as the disease progresses; the respiration becomes difficult and embarrassed, and there is cough with a tenacious, dark colored, or bloody expectoration. It is through the examination of this expectoration that the diagnosis is most easily made, as, spread upon a slide, stained and examined under the microscope, the presence of the plague bacillus in large numbers is at once established. The bacillus is not in pure culture, but is accompanied by diplococci, staphylococci, and streptococci, and in making the diagnosis by this method the property of the plague bacillus of completely decolorizing by the method of Gram must be borne in mind.

Post-mortem, the pneumonia is found to be generally lobular or disseminated in character, though it is sometimes lobar, sometimes involves a whole lung, or may indeed involve both lungs.

The general characteristic of the lesions of plague is a tendency to hemorrhages, either into the parenchyma of the spleen or kidneys, the subdural and arachnoid spaces, the spinal cord, or into the loose connective tissue of various regions of the body.

This tendency to hemorrhages would seem to be a manifestation of the peculiar properties of the toxins formed by the plague bacillus in the process of growth, as it has been observed alike in animals subjected to inoculations with the culture of the bacillus and its isolated toxins.

Among the sequelæ of the plague may be mentioned as most frequent,

long continued suppuration of glands, boils, and carbuncles, and eruptive diseases of the skin, and paralyses, sometimes of a particular set of muscles, sometimes of the lower and sometimes of the upper extremities. These manifestations may persist, or the affected muscles may gradually acquire strength and tone. These manifestations may be accounted for as to the suppurations by the fact that the plague bacillus is usually accompanied by the organisms of suppuration; as to the paralyses by the above-mentioned tendency to hemorrhages into the meninges and spinal cord.

Viability of the plague bacillus.—It would seem that the bacillus of plague, while not as sensitive to desiccation as the cholera spirillum, still loses its virulence by drying, and that to retain its virulence it requires the action of both heat and moisture. In ordinary water it will retain its activity for some time, but its existence in sterilized water seems to be limited to a period of from twenty-four to forty-eight hours. The presence of organic matter, animal or vegetable, and in a state of decomposition, would seem to furnish the most favorable nidus for its growth, which will account for its more or less prolonged existence in Oriental countries, and the comparative rarity of its appearance in Europe since the existence of modern and improved hygienic conditions. This does not mean, however, as was maintained by some at the Venice conference, that filth and crowding are alone responsible for the disease. The malady is preeminently of bacterial origin, and wherever the microbe is found, there the plague is likely to develop.

Serum therapy and preventive inoculation.—This branch of the subject I approach with considerable reluctance, for the reason that the serum therapy has not in the Bombay epidemic given results as brilliant as were hoped for from the eminently successful experiments made upon a very small scale by Yersin in the epidemic at Hongkong. For this there are good and sufficient reasons, well understood by those best acquainted with the manufacture and preparation of the antipest serum. The figures will first be given, and explanations entered into afterwards. In the Bombay epidemic there have been used serums from two sources, the one prepared by Yersin at the Pasteur Institute at Saigon, the other prepared at the Pasteur Institute at Paris and forwarded to Yersin at Bombay. With the former serum the mortality of all cases treated amounted to 33 per cent; with the latter the mortality has been approximately 50 per cent. The total mortality of all cases in which the serum therapy was inaugurated prior to the systemic intoxication—that is to say, on the first or second day of the disease—is 12 per cent.

Compared with the mortality without the serum treatment, 90 to 95 per cent, there is nothing to be ashamed of even in these figures, but it is not the result that was hoped for. As a prophylactic measure the results have been much more favorable. It has proved in this respect eminently successful, but a point involved in some doubt is the length of the immunity conferred. In one case the disease manifested itself in a person constantly exposed forty-two days after the preventive inoculation. This would point to a desirability of inoculations for those exposed, as physicians and attendants, at intervals not exceeding thirty to thirty-five days.

Fortunately we are able to cite cases where the inoculation was instrumental in preventing the disease, and this, I think, should establish the principle that in future epidemics it will be just as rational and scientific to practice preventive inoculation as it is now customary to vaccinate those exposed to an infection of smallpox, with a view of preventing the spread of the disease.

I would beg to relate the following incident: The Bombay manager of the local branch of the Credit Lyonnaise resided with his wife, children, and a numerous retinue of native servants in a dwelling in an infected portion of the city. His little daughter was stricken with the pest in a virulent form; was treated with the serum, and made a rapid and uneventful recovery. As a precautionary measure the whole family were subjected to inoculation, and the same measure of treatment was offered to the native domestics. Some accepted and escaped infection, while 6 who declined on the ground of religious scruples were all stricken, and 5 died. It seems that a more crucial test could not have been devised, or a more triumphant vindication obtained.

I will endeavor now to briefly explain why the therapeutic results obtained have not been more brilliant and the success more uniform.

In the first place, the epidemic has been largely confined to the natives, a class notoriously suspicious and superstitious. It has been only with the greatest difficulty that they have been persuaded to accept the protective inoculation, and when stricken with the pest, their religious scruples have often led them to decline the serum therapy until almost moribund. These cases have, of course, only served to reduce the ratio of recoveries to treatments, and to bring the method into disrepute among those prone to criticise and sneer, of whom unfortunately there have been too many in high places during this epidemic.

Secondly, to be perfectly frank, the fault has been in the serum itself, as can thus be explained: The serum prepared by Yersin at Saigon had not only a strong immunizing power, but also very high antitoxic or curative powers, as is conclusively proved by the results in his 23 cases treated at Hongkong. Unfortunately, the supply was small; Yersin departed for Bombay and an unfortunate accident in his laboratory prevented the continuance of this supply and the further treatment and preparation of his already immunized and seasoned horses. Recourse, therefore, had to be had to serum prepared in the Pasteur Institute in Paris. A large demand had not been anticipated here, and the supply on hand was also small, but in the belief that even a weak serum was better than none, there was issued to Dr. Yersin a quantity of serum which was known to have a high immunizing, but a comparatively low antitoxic or curative power. This is, in brief, the whole explanation. Every nerve is being strained to produce a stronger serum, but it is a matter which, in the very nature of things, takes a long time, and with a demand constantly exceeding the supply, it is impossible at this time to do better, though, if only sufficient time is allowed, there is no shadow of a doubt that a product will be reached whose potency will be a perfect vindication of the faith of such men as Professor Roux and his assistants. The technical reason in brief is the following: If a horse is injected intra-peritoneally with a culture of the plague bacillus, killed by exposure to heat, the animal in time acquires a certain immunity to these injections, and his serum is found to have certain preventive properties, viz, it will protect an animal into which it is injected against a culture of the plague bacillus; in other words it is preventive or prophylactic. This result has been arrived at by the action of the toxins contained in the killed culture, but it is to be borne in mind that the toxine is not in a soluble condition, but it is largely held enveloped in the bodies of the dead microbes. On the contrary, if the horse is injected with a live culture of plague, or a soluble toxine, and intravenously instead of intra-peritoneally, an immunity will be established, and the serum of the animal will be found to have not only an immunizing power as before, but in addi-

tion an antitoxic or curative power, that is to say, it will protect an animal against the toxins of plague, or the animal having been inoculated with plague, it will exert its curative or antitoxic influence. The difference is one of degree and not of kind. Every antitoxic serum is immunizing to a high degree, but the reverse does not hold good. It can therefore be laid down as a general rule that to prepare an immunizing serum the injection of killed culture or enveloped toxine is sufficient, while to prepare an antitoxic one, either the culture must be living, or the toxins in a soluble form and injected into a vein. Hence the difficulty; it is a most complex problem to dissolve the cellulose envelope of the microbe and set free its toxine without producing a chemical change in the product, and the matter is under continual experiment. That it will be solved eventually there is no doubt, but in the meantime the horses have to be treated with live culture, and the process is one requiring great caution and care, as accidents not infrequently happen, and the treatment of the horse has to be suspended. It will thus be seen that the whole matter is one involved in a great deal of difficulty, and requiring much earnest thought and work for its solution.

Nevertheless, I do not think it possible at this time to overrate the importance of the study of the toxins and antitoxines of the infectious and contagious diseases, as, to my mind, upon its development rests the whole future of preventive medicine. The study is at once fascinating and discouraging, for new difficulties constantly arise to take the place of those which have been overcome by laborious effort.

I have the honor, sir, to remain, very respectfully, yours,

H. D. GEDDINGS,

Passed Assistant Surgeon, U. S. M. H. S.

Yellow fever on the German bark Zion.

[Telegram.]

LEWES, DEL., June 24, 1897.

German bark *Zion*, forty days from Rio, in ballast, 15 crew, all well, arrived this afternoon. Had 2 cases yellow at Rio and 2 en route. Ordered to New York and proceeded without pratique; quarantined while here.

WERTENBAKER,

Passed Assistant Surgeon, U. S. M. H. S.

Plague at Jedda and Mecca.

77-79 RUE NOTRE DAME DES CHAMPS,

Paris, France, June 15, 1897.

SIR: In confirmation of my cablegram of the 9th instant announcing rumors of the existence of the plague at Jedda and Mecca, I have the honor to inform you that the news of the existence of plague at Jedda has been officially confirmed. Mecca is still in doubt, though there is little hope that, having reached the seaport, Mecca will escape a visitation. News has also been received here of the appearance of the plague in certain places upon the Chinese frontier, and ere this, I suppose, you have the information as to the outbreak in Formosa. The disease, therefore, appears to be making rapid extensions.

Very respectfully,

H. D. GEDDINGS,

Passed Assistant Surgeon, U. S. M. H. S.